IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
TYLER DIVISION

POZEN INC.	§	
	§	
Plaintiff,	§	
	§	**CASE NO. 6:08 CV 437**
vs.	§	**PATENT CASE**
	§	
PAR PHARMACEUTICAL, INC., ALPHAPHARM PTY LTD., TEVA PHARMACEUTICALS USA INC., DR. REDDY'S LABS., INC.	§	**CONSOLIDATED WITH CASE NO. 6:09 CV 3 AND CASE NO. 6:09 CV 182**
	§	
Defendants.	§	
	§	

FINDINGS OF FACT AND CONCLUSIONS OF LAW

This case involves a dispute over obtaining approval to market and sell generic drugs under the Hatch-Waxman Act. Pozen Inc. ("Pozen") filed suit against Defendants Par Pharmaceutical Inc. ("Par"), Alphapharm Pty Ltd. ("Alphapharm"), and Dr. Reddy's Laboratories, Inc. ("DRL") for patent infringement.[1] The case was tried on the merits without a jury and was taken under submission. The Court has considered the testimony, exhibits, arguments of counsel, and supporting memoranda, and details its Findings of Fact and Conclusions of Law below pursuant to Federal Rule of Civil Procedure 52(a).[2]

I. BACKGROUND

Pozen is a pharmaceutical company founded by Dr. John Plachetka, who developed a migraine therapy that was patented and approved by the Food and Drug Administration ("FDA").

[1] Pozen also sued Teva Pharmaceuticals USA, Inc. ("Teva") for infringement of the same patents-in-suit; however, Pozen and Teva entered into a settlement agreement, and Pozen's claims were dismissed without prejudice. *See* Docket No. 258.

[2] To the extent that any conclusion of law is deemed to be a finding of fact, it is adopted as such; and likewise, any finding of fact that is deemed to be a conclusion of law is so adopted.

The migraine therapy, which is marketed as Treximet, combines sumatriptan with naproxen in a single tablet.

Migraines are a chronic neurological disorder that cause various symptoms, including throbbing headache pain, photophobia (light sensitivity), phobophobia (sound sensitivity), and nausea. These symptoms can be intense and debilitating and can prevent a migraine sufferer from participating in normal, daily activities. 10/12/2010 A.M. TT at 70:20-72:5. While the specific underlying cause is unknown, vascular and neurological changes are attributed to migraines. Generally, vasodilation (enlargement of the blood vessels) stimulates the innervating nerve fibers, which leads to inflammation and subsequent pain. *Id.* at 74:17-76:3.

In the early 1980's, using a protocol commonly referred to as "step care," migraines sufferers were instructed to first take an analgesic (pain killer) to treat their migraine symptoms. If the symptoms did not subside within a few hours, patients were instructed to take a second, more potent medication such as a ergot alkaloid (a vasoconstrictor) or a narcotic. *Id.* at 72:6-73:25. However, these medications were insufficient because they treated the migraine symptoms and not the migraine mechanisms.

In the late 1980's, GlaxoSmithKline ("GSK") began developing sumatriptan, the first drug specifically targeting migraine pathway mechanisms. *Id*. at 76:4-77:16. Sumatriptan acts as an agonist to receptors in cranial arteries and veins, thus reducing the vascular inflammation that occurs with migraines.[3] *Id*. Sumatriptan was widely accepted as an effective medicine for migraines and

[3] Specifically, sumatriptan is a 5-HT receptor agonist that mediates vasoconstriction of the human basilar artery and vasculature of human dura mater, which correlates with the relief of migraine headaches. In addition to vasoconstriction, sumatriptan decreases the activity of the trigeminal nerve, which innervates cranial blood vessels, contributing to its antimigrainous effect. *See* PTX 214 at 259514.

adopted as the preferred secondary medication in the "step care" treatment of migraines. *Id.* at 77:19-78:7.

While sumatriptan was hailed as a revolution in migraine therapy, it did not prevent migraine symptoms from reoccurring. To address this relapse, patients were instructed to re-treat their migraine symptoms with an additional administration of only sumatriptan. Thus, the predominate two step care therapy evolved into a monotherapy approach using repeated treatments of sumatriptan. *Id*. at 78:22-81:22. But the sumatriptan monotherapy still failed to quash relapse, so further research and efforts were poured into finding a solution to this problem. Given its effectiveness in treating migraine symptoms, the industry used sumatriptan as a template and focused on finding longer-lasting, more potent triptan-related therapies. These therapies were generally known as second generation triptans. *Id*. at 81:14-82:14.

Although the limelight was on further advancing triptan-related monotherapies, Dr. Plachetka developed an alternate theory for treating migraine relapse. Instead of additional research on sumatriptan therapies, Dr. Plachetka focused on the inflammation outside the blood vessel that was unaffected by sumatriptan. *Id*. at 84:24-86:21. This approach was unconventional because the art taught that sumatriptan effectively blocked inflammation. *Id*. However, Dr. Plachetka believed that migraine relapse results from a biological mechanism distinct from the mechanisms triptan addresses, and he recognized that a different therapy must be used to combat migraine recurrence. *Id.* As such, Dr. Plachetka reasoned that, to target and stop the full migraine process, sumatriptan must be simultaneously delivered with a second drug that targets this alternate, relapse causing mechanism. *Id*. at 88:8-88:19. Accordingly, Dr. Plachetka chose naproxen, a well known anti-inflammatory, to address residual inflammation. *Id.* at 89:1-12. He hypothesized that

simultaneously dosing naproxen with sumatriptan would have a synergistic result and resolve both the initial migraine and reoccurring migraine symptoms. *Id.* at 88:8-89:15.

To illustrate, Dr. Plachetka's solution is analogous to dousing a campfire. Sumatriptan acts like dumping a bucket of water on a roaring flame. However effective, there may be embers untouched by the water. Those embers, like inflammation, can reignite the blaze and cause a relapse of migraine symptoms. Seeing that sumatriptan worked before, the industry continued to throw water at the flame, with the development of second generation triptans. Noticing the inadequacies of this continued method, Dr. Plachetka recognized an additional, established way to extinguish the embers of inflammation, with naproxen. *Id.* at 87:3-22. By combining naproxen with sumatriptan in a single dose, Dr. Plachetka essentially kicked dirt over the smoldering ashes and smothered the migraine symptoms.

While Dr. Plachetka was committed to the combination therapy of naproxen and sumatriptan, the concept was unsupported by the art and industry leaders. Naproxen was not an FDA approved treatment for migraines; at most, it was viewed as a weak analgesic used to address headache pain. *Id.* at 90:12-91:10. In fact, GSK initially rejected Dr. Plachetka's concept of simultaneous dosing of naproxen sodium with sumatriptan to mitigate migraine relapse. *Id.* at 97:11-98:7. Dr. Plachetka subsequently formed his own company, Pozen, to develop the product and bring it to market.

Dr. Plachetka and Pozen conducted clinical studies to prove the combination of sumatriptan and naproxen was safe and effective to reduce relapse and produce longer lasting efficacy to migraine sufferers. *Id.* at 98:17-102:9; 10/12/10 P.M. at 3:8-5:5; JTX 9, 72, 73, 76, 141, 142 (Treximet clinical studies and reports). The studies showed that simultaneous administration of sumatriptan and naproxen not only treats migraines more effectively than sumatriptan or naproxen

alone, it is also effective in preventing the migraine from returning within the first twenty-four hours. *Id.* Following the success of the clinical trials, GSK chose to license the therapy, Treximet, and became Pozen's marketing partner, licensee, and exclusive distributor in the United States. 10/12/10 P.M. at 5:6-7:1; PTX 498.

To obtain approval for Treximet, Pozen filed a New Drug Application ("NDA") with the FDA. Pozen's NDA included examples of the proposed label for the drug and the clinical data demonstrating that the drug is safe and effective for use. *See* 21 U.S.C. § 355 (b)(1)(A), (b)(1)(F). Pozen listed U.S. Patent Nos. 6,060,499 ("the '499 patent"), 6,586,458 ("the '458 patent"), and 7,332,183 ("the '183 patent") (collectively "the patents-in-suit") in its NDA as covering Treximet. *See id*. § 355 (b)(1)(G). On April 15, 2008, the FDA approved Treximet for the acute treatment of migraine attacks.

Par, Alphapharm, and DRL (collectively "Defendants") filed Abbreviated New Drug Applications ("ANDAs") with the FDA, seeking approval to sell generic copies of Treximet before the expiration of Pozen's patents. *See* 21 U.S.C. § 355 (b)(2), (j)(2). Defendants' ANDAs included statements that the method of administration, the dosage form, pharmaceutical strength, and proposed labeling for the generics is the same as for Treximet. *Id*. at 21 U.S.C. § 355 (j)(2). Defendants' ANDAs also certified that Pozen's '499, '458, and '183 patents are invalid and/or will not be infringed by the manufacture, use, or sale of the generics. *Id.* at (j)(2)(A)(vii)((I)-(IV); *see also AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1045-46 (Fed. Cir. 2010).

Based on Defendants' ANDA filings, Pozen filed suit against Par and later amended its Complaint to add Alphapharm and DRL. Pozen's lawsuit triggered a 30-month stay of Defendants' FDA's approval. *See* 21 U.S.C. § 355(j)(5)(B). In its prayer for relief, Pozen requests the Court

enter an order determining that Defendants' ANDA products infringe Pozen's '499, '458, and '183 patents. Pozen also requests the Court set the effective dates of the approval of Defendants' ANDAs after the patents-in-suit expire and permanently enjoin Defendants from making, using, selling, offering to sell or importing into the United States their ANDA products until the patents-in-suit expire. *See* 35 U.S.C. § 271(e)(4)(A)-(B).

Following a *Markman* hearing, the Court adopted Magistrate Judge Love's Order denying Defendants' Motion for Summary Judgment of Indefiniteness and construing claim terms. The Court conducted a five-day bench trial regarding Pozen's infringement and Defendants' noninfringement, invalidity, and unenforcability allegations.

II. INFRINGEMENT

Pozen alleges that: 1) Defendants' ANDA products infringe claim 15, which depends on claim 5, of the '499 patent; 2) Defendants' ANDA products infringe claims 11, 12, and 24, which depend on claim 3, and claims 26, 27, 29, and 30 of the '458 patent; and 3) Par's and DRL's ANDA products infringe claim 2 of the '183 patent under the doctrine of equivalents.

A. Legal Standard

35 U.S.C. § 271(e)(2)(A) provides that filing an ANDA constitutes an artificial act of infringement for which the ANDA filer may be liable for direct infringement or for inducement to infringe. *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003). This "artificial" act of infringement creates case-or-controversy jurisdiction to enable the resolution of an infringement dispute before the ANDA applicant has actually made or marketed the proposed product. *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997). To determine infringement, the proper inquiry is whether, if the ANDA product were put on the market, it would

infringe the patent, either directly or through inducement. *Warner-Lambert*, 316 F.3d at 1366.

A person is liable for direct infringement if he "without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefore." 35 U.S.C. § 271(a). Indirect infringement occurs where a person induces infringement or contributes to infringement. *Id.* at § 271(b),(c). Direct infringement must be established as a predicate for each act of indirect infringement. *See Dynacore Holding Corp. v. U.S. Philips Corp.*, 363 F.3d 1263, 1272 (Fed. Cir. 2004) ("Indirect infringement . . . can only arise in the presence of direct infringement, though the direct infringer is typically someone other than the defendant accused of indirect infringement."). To show inducement, the patentee must establish evidence of culpable conduct directed toward encouraging another's infringement. *See DSU Med. Corp v. JMS Co.,* 471 F.3d 1293, 1304 (Fed. Cir. 2006) (en banc in relevant part). To prove infringement, the patent holder bears the burden of proof to show the presence of every element or its equivalent in the accused product by a preponderance of the evidence. *Lemelson v. United States*, 752 F.2d 1538, 1551 (Fed. Cir. 1985).

To find infringement under the doctrine of equivalents, any differences between the claimed invention and the accused product must be insubstantial. *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 608 (1950). The "essential inquiry" in any determination under the equivalents doctrine is whether "the accused product or process contain[s] elements identical or equivalent to each claimed element of the patented invention." *See Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 40 (1997). One way of proving infringement under the doctrine of equivalents "is by showing on a limitation by limitation basis that the accused product performs substantially the same function in substantially the same way with substantially the same result as

each claim limitation of the patented product." *Id.* at 39-40. However, "'[e]quivalence, in the patent law, is not the prisoner of a formula and is not an absolute to be considered in a vacuum.'" *Id.* at 24-25 (quoting *Graver Tank*, 339 U.S. at 609).

B. The '499 and '458 Patents

The '499 and '458 patents are derived from the same parent application. The '458 patent issued from an application that was a continuation-in-part of the application that issued as the '499 patent. Both the '499 and '458 patents disclose a treatment model that provides relief for migraine headaches through the simultaneous administration of two therapeutic agents in a single tablet: (1) sumatriptan and (2) the long-acting, non-steroidal anti-inflammatory agent ("LA-NSAID") naproxen. Sumatriptan is targeted at reducing already-existing inflammation, and naproxen is targeted at reducing residual inflammation. The patents provide that the combination of these drugs produces "longer lasting efficacy" than the administration of either drug alone. '458 patent at 2:18–22; '499 patent at 4:49-62. Many of the '499 and '458 patents' elements overlap with slight variations in claim language.

1. The Asserted '499 Patent Claims

The '499 patent generally requires unit doses, comprising sumatriptan and the LA-NSAID naproxen, and a finished pharmaceutical container. Pozen asserts Defendants' ANDA products directly infringe claim 15, which depends on claim 5, of the '499 patent. Pozen also asserts Defendants are liable for inducing infringement. The asserted claim recites:

> 5. A *therapeutic package* for dispensing to, or for use in dispensing to, a migraine patient, which comprises:
> (a) one or more unit doses, each such unit dose comprising:
> (i) a 5-HT agonist and

> (ii) a long-acting, non-steroidal, anti-inflammatory drug (LA-NSAID); wherein the respective amounts of said 5-HT agonist and said LA-NSAID in said unit dose are effective, upon concomitant administration to said patient of one or more of said unit doses, to reduce migraine relapse or produce longer lasting efficacy compared to the administration of said 5-HT agonist in the absence of said LA-NSAID or the administration of said LA-NSAID in the absence of said 5-HT agonist, and
>
> (b) *a finished pharmaceutical container therefor, said container containing said unit dose or unit doses, said container further containing or comprising labeling directing the use of said package in the treatment of migraine*.
>
> 15. The improvement, method, or composition of claims 1, 2, 3, 4, 5, 6, 7, or 8, wherein said 5-HT agonist is sumatriptan, said LA-NSAID is naproxen and the unit dosage form is an oral unit dosage form comprising sumatriptan in an amount greater than 15 mg, and naproxen in an amount greater than 200 mg.

'499 patent at 14:1-19; 15:12-17 (disputed portions emphasized). Defendants stipulated to meeting several of the asserted '499 patent claim limitations.[4] The parties' infringement arguments for the '499 patent focus on: 1) "therapeutic package" and 2) "finished pharmaceutical container therefor, said container containing said unit dose or unit doses, said container further containing or comprising labeling directing the use of said package in the treatment of migraine."

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[4] Par stipulated to the following limitations: a 5-HT agonist (claim 5); wherein said 5-HT agonist is sumatriptan (claim 15) sumatriptan in an amount of greater than 15 mg (claim 15); and a long-acting, non- steroidal, anti-inflammatory drug (LA-NSAID) (claim 5). *See* Docket No. 339.

Alphapharm stipulated to the following limitations: a 5-HT agonist (claim 5); wherein said 5-HT agonist is sumatriptan (claim 15), sumatriptan in an amount of greater than 15 mg (claim 15); a long-acting, non- steroidal, anti-inflammatory drug (LA-NSAID) (claim 5). *See* Docket No. 338.

DRL stipulated to the following limitations: for dispensing to, or for use in dispensing to, a migraine patient (claim 5), each unit dose comprising: (i) a 5-HT agonist and (ii) a long acting, non-steroidal, anti-inflammatory drug (LA-NSAID) (claim 5), a 5-HT agonist (claim 5); wherein said 5-HT agonist is sumatriptan (claim 15), sumatriptan in an amount of greater than 15 mg (claim 15); a long-acting, non- steroidal, anti-inflammatory drug (LA-NSAID) (claim 5), wherein said LA-SAID is naproxen, said naproxen in an amount greater than 200 mg (claim 15), oral unit dosage form (claim 15). *See* Docket No. 339.

2. Direct Infringement Analysis of the '499 Patent

a. Therapeutic Package

The claim term "therapeutic package" appears in the preamble. The Court has not previously construed the term, and the parties dispute its scope and definition. Defendants argue "therapeutic package" is not a term widely used in the art, but its plain language "means packaging that enhances patient therapy by promoting compliant use" and "implies something therapeutic about the packaging itself." Docket No. 400 at 45-46, *see also* 10/13/10 P.M. TT at 47:23-52-19. Defendants contend they do not satisfy the limitation because it requires more than an ordinary pill bottle, reasoning exemplary therapeutic packages include packaging of birth control pills and Z-packs. *Id*. Pozen contends the plain and customary meaning of "therapeutic package" is a "package for delivery of therapy."

A preamble is not limiting if it does not recite essential structure or steps, or is not necessary to give life, meaning, and vitality to the claim. *Poly–Am., L.P. v. GSE Lining Tech*., *Inc.,* 383 F.3d 1303, 1309 (Fed. Cir. 2004). Nor is a preamble limiting "where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention." *Rowe v. Dror*, 112 F.3d 473, 478 (Fed. Cir.1997). A court reviews the entirety of the patent to gain an understanding of what the inventors actually invented and intended to encompass by the claim to determine what effect preamble language should be given. *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir.1989).

The term "therapeutic package" is not essential to understand the limitations in the claim body; rather, the elements provided in claim 5 define the scope of Pozen's invention. Defendants' arguments incorrectly skew Pozen's invention toward the packaging, rather than the entirety of the

invention. However, in the '499 patent, Pozen sought to invent and claim: 1) unit dose of sumatriptan and naproxen; and 2) a finished pharmaceutical container that contains the unit dosages and is labeled to direct the use of the package in migraine treatment. '499 patent at 14:1-19. Pozen provided these complete parameters of its invention in the claim body. Thus, the term "therapeutic package" is illustrative and does not add a limitation that is not already present in the claim, nor is it necessary to give meaning to the claim.

Even if one of ordinary skill in the art viewed "therapeutic package" as limiting, the '499 patent does not support Defendants' interpretation. Claim 5 of the '499 patent describes the elements that make up the "therapeutic package": unit doses and finished pharmaceutical containers. '499 patent at 14:1-19. The claim uses the term "package" in the normal sense of any outer container with specified contents. The plain language of the term does not require the packaging to actively direct therapy or improve compliant use, and the '499 patent does not support the importation of such limitations. If Pozen had intended to further define the configuration of the container portion of the package it could easily have done so—but it did not. The use of the term "therapeutic," as noted above, implies nothing more than that the complete package is intended for use in therapy—the adjective "therapeutic" does not imply any particular structure for the container portion of the package. Thus, even if this term is a limitation, one of ordinary skill in the art would understand the plain and ordinary meaning of "therapeutic package" as simply a package for use in therapy. *See* 10/12/10 P.M. TT at 129:13-130:12.

The '499 patent does not support Defendants' attempt to limit the term to particular type of packaging. Defendants contend that the blister packaging and instructions used in birth control pills and Z-packs are examples of "therapeutic packaging" and distinguish their ANDA products from

these examples. *See* 10/13/10 P.M. TT 50:20-55:7. Defendants' examples, however, are not disclosed by the specification as exemplary embodiments of the invention. In fact, the specification and claims do not limit the term to a particular embodiment, nor do they limit it to Defendants' examples. Thus, even if "therapeutic package" was limiting, Defendants' ANDA products satisfy this limitation because they are 1) unit doses of sumatriptan and naproxen and 2) a finished pharmaceutical container that contains the unit dosages and is labeled to direct the use of the package in migraine treatment, as further described below.

b. Label Limitation

Claim 5 requires "a finished pharmaceutical container therefor, said container containing said unit dose or unit doses, said container further containing or comprising labeling directing the use of said package in the treatment of migraine." '499 patent at 14:1-19. The Court construed "finished pharmaceutical container" to mean "a container, ready for packaging, shipment, or sale, that contains unit dose(s) or unit dosage form(s) and labeling directing the use of the therapeutic package in the treatment of migraine headache." Docket No. 259 at 10.

The parties specifically dispute whether Defendants' ANDA products satisfy the claim's labeling requirement. Pozen asserts Defendants' ANDA products have "labels that direct the patient to the medication guide or package insert prescribing information, which in turn directs the patient to take a tablet (one component of the therapeutic package) to treat a migraine." Docket No. 401 at 10-11. Defendants assert their labels do not have instructions for product use and further argue that any language on the label is intended for the physician or pharmacist—not the patient. 10/13/11 P.M. TT at 57:21-59:1. Defendants also contend their package inserts and medication guides direct

the use of the tablet and do not specifically direct the use of the packaging for migraine treatment. Docket No. 400 at 50.

These narrow interpretations are unsupported by the '499 patent. The claims do not require guidance on the use of the container, as Defendants imply, but only directions on use of "said package in the treatment of [a] migraine" and, as noted above, the "package" is defined as both doses and the container. Accordingly, the '499 patent does not support Defendants' argument that the labeling must be limited to directing the use of the packaging that holds the medication and not the medication itself. Nor does the '499 patent specify that the labeling must be directed to the patient only, and not to the physician, nurse practitioner, or pharmacist. Also contrary to Defendants' arguments, the patent does not require that the language of the label must specifically provide the usage directions and cannot reference any accompanying information, such as a medication guide or package insert. In other words, Defendants do not avoid infringement simply because details of those directions are not printed on the label. Moreover, Defendants' labels reference the accompanying inserts which provide additional information and instruction. Accordingly, Defendants' non-infringement arguments based on this term are too narrow and are unsupported by the patent.

Defendants' ANDA products are described by their proposed package inserts, labeling, and by the testimony of their corporate representatives.[5] While their labeling varies slightly, each Defendant's ANDA product has "labeling directing the use of said package in the treatment of migraine." Par's ANDA label provides "USUAL DOSAGE: See Prescribing Information for

[5] *See* Par: PTX 109; PTX 108; 10/13/10 A.M. TT at 83:12-87:12; 88:24-89:20; Alphapharm: PTX 204; PTX 234; PTX 236; 10/13/10 A.M. TT at 95:17-101:11; DRL: PTX 132, PTX 240, 10/13/10 A.M. TT at 90:11-93:24.

complete storage and dosage information." PTX 108 at 9891. As required by federal law, the label also references the Medication Guide that is dispensed with Par's ANDA product. *Id*. Par's Medication Guide provides information to the patient about its product, including its use for the treatment of migraine attacks and instructions on how to take the tablets. *Id*. at 9894; *see also* PTX 109 at 9907, 9937-38, 9942; 10/13/10 A.M. TT at 84:13-16, 87:6-8; 10/12/10 P.M. TT at 131:2-122:16. Alphapharm's ANDA product instructs "For dosage and other prescribing information see accompanying product literature," "Pharmacist: Dispense Medication Guide with drug product," and will also include a medication guide. PTX 236 at 92104; *see also* 10/13/10 P.M. TT at 63:5-64:13. Alphapharm's labeling also directs the patient in the use of the product by referencing the accompanying product literature and medication guide. PTX 204 at 92112, 92118; PTX 234 at 92434; 10/13/10 P.M. 63:5-64:13. DRL's packaging is labeled "Usual Dosage: See Prescribing Information for complete dosage information." PTX 240. DRL's label also includes instructions on how to take the tablets, which is reiterated in its package inserts. *See* PTX 240 ("Tablet should not be split, crushed, or chewed."); PTX 132 at 59870. Like Par and Alphapharm, DRL's label directs the user to the accompanying information, which further instructs the therapeutic uses of its product. *See* PTX 132 at 59870, 59846. DRL's proposed package insert provides detailed information to the patient about its product and its use for the treatment of migraine attacks. *Id*.

Defendants' ANDA products also meet the remaining, undisputed portions of this element.[6] Accordingly, Defendants' ANDA products utilize a "a finished pharmaceutical container therefor, said container containing said unit dose or unit doses, said container further containing or comprising labeling directing the use of said package in the treatment of migraine."

c. Pharmaceutical Composition and Administration Limitations

Pozen contends Defendants' ANDA products meet claims 5 and 15's pharmaceutical and administration limitations.[7] Defendants did not specifically stipulate to these limitations and offer only a general protest that Pozen failed to show that their proposed ANDA products satisfy the limitations and improperly compared the ANDA products to Treximet instead of the claims. Contrary to Defendants' arguments, Pozen's presentation on infringement at trial included comparisons of the proposed ANDA products to the patents-in-suit, demonstrating that the accused products satisfy the remaining claim limitations as shown below.

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[6] Par's ANDA product is a pharmaceutical composition in a unit dosage form for a patient's oral consumption. *Id*. at 84:4-16; *see also* PTX 108 at 9891. The unit dose will be packaged in a container that is ready for packaging, shipment, or sale. *See* 10/13/10 A.M. TT at 83:12-84:1.

Alphapharm exports its ANDA product in bulk containers that will be repackaged for retail. PTX 234 at 92434. These bulk products are ready for packaging, shipment, or sale and dispensed to patients. *Id.* Alphapharm's ANDA retail products will likewise contain the unit dosages and are ready for packaging, shipment, or sale. PTX 236 at 92104; *see also* 10/13/10 P.M. TT at 63:5-64:13.

DRL stipulated that its ANDA product meets the "finished pharmaceutical container" limitation. *See* Docket No. 340; *see also* 10/13/10 A.M. TT at 90:16-91:5.

[7] The Court construed the term "concomitant administration" and its permutations in the '499 patent as "simultaneous administration" or "administration of a second drug for migraine relief while a first drug for migraine relief is present in a therapeutically effective amount," or "administration of a 5-HT agonist and NSAID such that the effective plasma levels of the NSAID will be present in a subject from about one hour to about 12–24 hours after the onset of migraine or onset of precursor symptoms of a migraine." Docket No. 259.

Defendants' ANDA products are a pharmaceutical composition that are in an oral unit dosage.[8] The sumatriptan and naproxen doses are provided in a single tablet, intended for oral administration to a migraine patient and thus administered simultaneously.[9] Therefore, Defendants' ANDA products meet the "concomitant administration" required by the '499 patent.

Claims 5 and 15 also require that the simultaneous delivery of sumatriptan and naproxen reduces migraine relapse or produces a longer lasting efficacy as compared to the administration of either alone. There is extensive clinical trial data showing that the simultaneous administration of naproxen and sumatriptan, as in Defendants' proposed ANDA tablets, produces a longer lasting effect and reduces migraine relapse.[10] This longer lasting efficacy is further confirmed by Defendants' representations to the FDA that their ANDA products are pharmaceutically equivalent,

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[8] Par: 10/13/10 A.M. TT at 84:4-16; *see also* PTX 108 at 9891; Alphapharm: 10/13/10 A.M. TT at 95:17-96:25; *see also* PTX 204 at 92112; DRL: Docket No. 340; *see also* PTX 657; PTX 661. Defendants' ANDA products are composed of 5-HT, sumatriptan in an amount greater than 15 mg, and an LA-NSAID, naproxen in an amount greater than 200 mg. *See* Par: Docket No. 339; 10/13/10 A.M. TT at 85:24-87:1; PTX 108 at 98; PTX 109 at 9899; PTX 659; Alphapharm: Docket No. 338; 10/13/10 A.M. TT at 96:1-99:19; PTX 204 at 92112; PTX 658; DRL: Docket No. 339; 10/13/10 A.M. TT at 91:13-19; PTX 657; PTX 661.

[9] *See* Par: PTX 109 at 9899; *see also* 10/12/10 P.M. TT at 121:19-122:1; Alphapharm: 10/13/10 A.M. TT at 96:17-96:22; PTX 204 at 92112; DRL: Docket No. 339; 10/13/10 A.M. TT at 91:6-12; PTX 132 at 59846.

[10] *See* 10/13/10 A.M. TT at 22:12-22:17; 10/12/10 P.M. TT at 21:18-22:9; PTX 260 (Krymchantowski, AV, *Naproxen Sodium Decreases Migraine Recurrence when Administered with Sumatriptan*, Arq Neuropsiquiatr 58(2-B): 428-430 (2000)); JTX 9 (Smith, Timothy, et al., *Sumatriptan and Naproxen Sodium for the Acute Treatment of Migraine*, Headache at 983-991 (September 2005)); JTX 10 (Brandes, et al., *Sumatriptan-Naproxen for Acute Treatment of Migraine*, JAMA 297(13): 1443-54 (2007)). In addition, Pozen's pilot study and Phase II studies demonstrated a reduction in migraine relapse and longer lasting efficacy in its simultaneous administration of naproxen and sumatriptan. *See* JTX 72 (Protocol No. MT400-201); JTX 141 (MT400-202 Protocol); PTX 565 (MT400-204 Report); *see also* 10/12/10 P.M. TT at 3:8-4:19, 122:13-123:10; 10/12/10 A.M. TT at 98:12-102:6. This result was again demonstrated in Pozen's Phase III clinical trials on Treximet. JTX 76 (Final Clinical Study Report for MT 400-301); JTX 142 (MT400-302 Study Report); *see also* 10/12/10 P.M. at 7:19-8:20, 9:7-9:2, 9:23-10:11. Moreover, articles regarding this improved efficacy have been published in various trade journals. *See* PTX 288 (Cleves and Tepper et al., *Sumatriptan/Naproxen Sodium Combination for Treatment of Migraine*, Expert Reviews Neurother 8(9): 1289-1297 (2008)); PTX 628 (Tepper & Spears, *Acute Treatment of Migraine*, Neurol. Clin. 27: 417-427 (2009)); *see also* 10/13/10 A.M. TT at 9:8-9:20; 32:3-32:11;10/12/10 P.M. at 11:25-12:7; 24:6-26:13.

therapeutically equivalent, and bioequivalent to Treximet.[11] For these reasons, Defendants' ANDA products meet the '499 limitation "to reduce migraine relapse or produce longer lasting efficacy compared to the administration of said 5-HT agonist in the absence of said LA-NSAID or the administration of said LA-NSAID in the absence of said 5-HT agonist." In sum, the Court finds by a preponderance of evidence that Defendants satisfy the remaining elements regarding the pharmaceutical composition and administration.

d. Conclusion

In conclusion, based on the evidence set forth above, Pozen has shown by a preponderance of the evidence that Par, Alphapharm, and DRL meet the limitations of claim 15, as dependant on claim 5, of the '499 patent. The Court finds Defendants' ANDA products directly infringe the ' 499 patent.

3. Indirect Infringement

In addition, Pozen asserts that Defendants' ANDA products induce infringement of claim 15 of the '499 patent. Defendants argue Pozen's assertions fail because it waived indirect infringement by not including the allegation in its Proposed Findings of Fact and Conclusions of Law. *See* Docket No. 306. Defendants also maintain that their products do not include a "therapeutic package" and

[11] DRL and Alphapharm's corporate representatives admitted their ANDA products are pharmaceutically equivalent to Treximet. 10/12/10 P.M. at 126:21-127:1; 127:11-21; *see* Par: PTX 228; PTX 109 at 9904-07; Alphapharm: PTX 204 at 92115-18; PTX 210; PTX 211; DRL: JTX 163 at 4388; PTX 132 at 59849-52; PTX 223; *see also* 10/12/10 P.M. at 125:13-125:22. The FDA defines pharmaceutical equivalents as generic drug products that have "the same active ingredient(s), are of the same dosage form, route of administration and are identical in strength or concentration." PTX 209 at 8369. Therapeutic equivalents are defined by the generic drug product's ability to have the same clinical effect as the pioneer (innovator) drug product. *Id*. Bioequivalent drug products have no significant differences in the rate and extent to which the active ingredients become available at the site of action (e.g. no significant differences in rate and extent of absorption). *Id*. These equivalents claims allow Defendants to rely on the Treximet clinical trial data to attest to the FDA the effectiveness of their ANDA products.

"labeling directing the use of said package in the treatment of migraine" and thus, cannot induce infringement.

Although Pozen did not include indirect infringement in its Proposed Findings of Facts and Conclusions of Law, the parties' Joint Final Pre-Trial Order included Pozen's allegation that Defendants indirectly infringed by inducement. *See* Docket No. 327. This disclosure provided Defendants with sufficient notice that Pozen was pursuing its indirect infringement claims. Accordingly, Pozen did not waive its inducement allegations.

Section 271(b) provides that "[w]hoever actively induces infringement of a patent shall be liable as an infringer." The Court's determination of direct infringement of claim 15 of the '499 patent establishes the predicate for indirect infringement. Pozen presented a preponderance of evidence that establishes Defendants' culpable conduct directed toward encouraging another's infringement. *See DSU Med. Corp*, 471 F.3d at 1304. This culpable conduct is established by Defendants' ANDAs filed with the FDA, which seek approval to manufacture, market, and sell their product. Moreover, as detailed above, these proposed ANDA products, specifically Defendants' proposed label and package inserts, demonstrate that Defendants intended to actively and knowingly abet others (e.g. patients) in an infringing use of their products. *See supra* at at Part II.B.2.b-c. Defendants also had the requisite knowledge of the patents-in-suit. *See Insituform Techs., Inc. v. Cat Contracting, Inc.*, 161 F.3d 688, 695 (Fed. Cir. 1998). Defendants knew of the '499 patent at least as early as when they filed their ANDAs with the FDA. *See* JTX 160. Accordingly, Pozen has shown by a preponderance of the evidence that Par, Alphapharm, and DRL induce infringement of the '499 patent.

4. Infringement of the '458 Patent

The '499 and '458 patents are derived from the same parent application, share substantially the same specification, and include many overlapping elements with slight changes in claim language. Pozen alleges that Defendants' ANDA products infringe claims 11, 12 and 24, which depend on claim 3, and claims 26, 27, 29, and 30 of the '458 patent.[12] Defendants have stipulated to meeting several of the asserted claim limitations of the '458 patent.[13] Defendants' briefing asserts

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[12] These claims generally require oral unit dose pharmaceutical compositions for treating migraine headaches. This oral unit dosage contains between 25 and 100 mg of the 5-HT agonist sumatriptan and between 200 and 600 mg of the LA-NSAID naproxen. The LA-NSAID has a pharmacokinetic half-life of at least four hours and a duration of action of at least six hours. The combination of sumatriptan and naproxen is administered simultaneously, thereby reducing migraine relapse or resulting in a longer lasting efficacy compared to either administered alone. To illustrate, claims 11 and 12, which depend on claim 3, require:

> 3. A pharmaceutical composition in unit dosage form, useful in treating a migraine headache patient, which comprises:
>
> (a) a 5-HT agonist, wherein said 5-HT agonist is a triptan; and
>
> (b) a long-acting, non-steroidal, anti-inflammatory drug (LA-NSAID), wherein said LA-NSAID has a pharmacokinetic half-life of at least 4 hours and a duration of action of at least 6 hours;
>
> wherein the respective amounts of said 5-HT agonist and said LA-NSAID in said composition are *effective, upon concomitant administration to said patient of one or more of said unit dosage forms of said composition, to produce longer lasting efficacy compared to the administration of said 5-HT agonist in the absence of said LA-NSAID or the administration of said LA-NSAID in the absence of said 5-HT agonist.*
>
> 11. The method or composition of any one of claims 1-5, wherein said LA-NSAID is naproxen or a pharmaceutically acceptable salt in an amount of greater than 200 mg.
>
> 12. The method or composition of any one of claims 1-5, wherein said 5-HT agonist is sumatriptan, and said LA-NSAID is naproxen in an oral unit dosage form comprising sumatriptan in an amount of greater than 25 mg and naproxen in an amount of greater than 200 mg.

'458 patent at 12:29-45 (disputed limitation italicized); 13:36-43.

[13] Par stipulated to the following limitations: 5-HT agonist is a triptan (claims 3, 25, and 28); wherein said 5-HT agonist is sumatriptan (claims 12, 26, and 29); sumatriptan in an amount of greater than 25 mg (claim 12); said sumatriptan is present in an amount of between 25 and 100 mg (claims 27 and 30); a long-acting, non-steroidal, anti-inflammatory drug (LA-NSAID) (claims 3, 25 and 28); wherein said LA-NSAID is naproxen or a pharmaceutically acceptable salt in an amount of greater than 200 mg (claim 11); wherein said LA-NSAID is selected from the group consisting of flurbiprofen, ketoprofen, naproxen, oxaprozin, etadolac, indomethacin, ketorolac, nabumetone, mefanamic acid, and piroxicam (claim 22); wherein said naproxen is in the form of a sodium salt (claim 24).

one noninfringement argument for the '458 patent: that Pozen improperly compared the proposed ANDA products to Treximet rather than the claims and thus failed to show Defendants meet the limitation requiring "effective, upon concomitant administration to said patient of one or more of said unit dosage forms of said composition, to produce longer lasting efficacy compared to the administration of said 5-HT agonist in the absence of said LA-NSAID or the administration of said LA-NSAID in the absence of said 5-HT agonist." *See* Docket No. 400; *see also* '458 patent at 12:29-45. Although the claim language slightly varies, this limitation is required by each of the asserted claims.

As previously addressed in the analysis of Defendants' infringement of the '499 patent, Pozen's presentation on infringement at trial included comparisons of the proposed ANDA products to the patents-in-suit, and Pozen proved by a preponderance of the evidence that Defendants' ANDA products satisfy all the limitations of the asserted '458 patent claims.[14]

Alphapharm stipulated to the following limitations: 5-HT agonist is a triptan (claims 3, 25, and 28); wherein said 5-HT agonist is sumatriptan (claims 12, 26, and 29); sumatriptan in an amount of greater than 25 mg (claim 12); said sumatriptan is present in an amount of between 25 and 100 mg (claims 27 and 30); a long-acting, non-steroidal, anti-inflammatory drug (LA-NSAID) (claims 3, 25, and 28); wherein said LA-NSAID is naproxen or a pharmaceutically acceptable salt in an amount of greater than 200 mg (claim 11); wherein said LA-NSAID is selected from the group consisting of flurbiprofen, ketoprofen, naproxen, oxaprozin, etadolac, indomethacin, ketorolac, nabumetone, mefanamic acid, and piroxicam (claim 22); wherein said naproxen is in the form of a sodium salt (claim 24).

DRL stipulated to the following limitations: a pharmaceutical composition (claims 11, 12, 24, 26, 27, 29, and 30); in an oral unit dosage form (claim 12); said pharmaceutical composition is suitable for oral administration (claims 27 and 30); useful in treating a migraine headache patient (claims 11, 12, 24, 26, 27, 29, and 30); a 5-HT agonist (claims 3, 25, and 28); 5-HT agonist is a triptan (claims 3, 25, and 28); wherein said 5-HT agonist is sumatriptan (claims 12, 26, and 29); sumatriptan in an amount of greater than 25 mg (claim 12); said sumatriptan is present in an amount of between 25 and 100 mg (claims 27 and 30); a long-acting, non-steroidal, anti-inflammatory drug (LA-NSAID) (claims 3, 25, and 28); wherein said LA-NSAID has a pharmacokinetic half-life of at least 4 hours and a duration of action of at least 6 hours (claims 3, 25, and 28); wherein said LA-NSAID is naproxen or a pharmaceutically acceptable salt in an amount of greater than 200 mg (claims 11 and 24); wherein said LA-NSAID is selected from the group consisting of flurbiprofen, ketoprofen, naproxen, oxaprozin, etadolac, indomethacin, ketorolac, nabumetone, mefanamic acid, and piroxicam (claim 22); wherein said naproxen is in the form of a sodium salt (claim 24); said naproxen is present in an amount of between 200 and 600 mg claims 27 and 30).

[14] Defendants proposed ANDA products are pharmaceutical compositions. *See* discussion and sources *supra* at Part II.B.2, C.2. Defendants' proposed ANDA products are in a unit dosage form of a single tablet for oral dosing that is useful in treating a migraine headache patient. *Id*. The tablet contains sumatriptan (5-HT agonist) and naproxen (LA-SAID) as the active ingredients. *Id*. The tablet contains naproxen sodium or a pharmaceutically acceptable salt.

C. The '183 Patent

The '183 patent discloses a unique tablet architecture to orally administer a combination of sumatriptan and naproxen. In this delivery model, the sumatriptan and naproxen are "segregated into separate layers" that dissolve in the stomach substantially independent of one another. '183 patent at 1:56–57. The specific oral dosage and the segregation of the therapeutic agents are intended to provide superior dissolution and absorption in the body. *Id*. at 1:60–62 ("The dosage forms of the invention have been found to have substantial advantages over others in terms of release properties, stability, and pharmacokinetic profile.").

1. The Asserted '183 Patent Claims

Pozen asserts Par's and DRL's ANDA products infringe claim 2 under the doctrine of equivalents. The asserted claim recites:

> 1. A multilayer pharmaceutical tablet comprising naproxen and a triptan and, wherein
>
> a) *substantially all of said triptan is in a first layer of said tablet and substantially all of said naproxen is in a second, separate layer*; and
> b) *said first layer and said second layer are in a side by side arrangement such that the dissolution of said naproxen occurs independently of said triptan*.
>
> 2. The tablet of claim 1, wherein said naproxen is in the form of naproxen sodium between 200 and 600 mg.

'183 patent at 18:30–39 (disputed limitations italicized).

Id. The amount of naproxen is between 200 and 600 mg. *See* 10/12/10 p.m. TT at 117:7-119:4; s*ee also* Par: PTX 109 at 9899; 10/13/10 a.m. TT at 85:24-87:5. Alphapharm: PTX 204 at 92112; 10/13/10 a.m. TT at 99:20-23. DRL: Docket No. 340. The naproxen in Defendants' proposed ANDA products has a pharmacokinetic half-life of at least four hours, and the action of the naproxen is at least six hours. *See* PTX 206 at 1358305-05; PTX 207 at 1358333; 10/12/10 p.m. TT at 118:10-119:9; *see also* Par: PTX 109 at 9900; 10/13/10 a.m. TT at 84:21-85:4. Alphapharm: PTX 204 at 92113; 10/13/10 a.m. TT at 98:13-25. DRL: Docket No. 340. The sumatriptan and naproxen in Defendants' ANDA products are contained in a single tablet, thus are administered simultaneously. *See* discussion and sources *supra* at Part II.B.2, C.2. This simultaneous single unit dose of sumatriptan and naproxen produces a longer lasting efficacy and reduce migraine relapse compared to either administered alone. *Id*.

2. Infringement Analysis of the '183 Patent

Par and DRL argue their ANDA products do not contain substantially all of their sumatriptan and naproxen in separate layers and that the layers are not in a side by side arrangement that achieve independent dissolution. Pozen concedes Par's and DRL's products do not literally infringe these disputed elements and relies on the function, way, result test under the doctrine of equivalents. However, Par and DRL contend that Pozen's reliance on the doctrine of equivalents improperly vitiates the Court's claim construction and further argue the claim language "substantially all" also prevents the application of the doctrine of equivalents.

The claim requires "*substantially all* of said triptan is in a first layer of said tablet and *substantially all* of said naproxen is in a second, separate layer." '183 patent at 18:30–39. The Court defined this as "at least 90%, and preferably greater than 95%, of the total triptan present in the tablet is included within one distinct layer and at least 90%, and preferably greater than 95%, of the naproxen present in the tablet is included within a second distinct layer." Docket No. 257 at 27. It is undisputed that Par's ANDA product contains 85% of naproxen in the second layer, and that DRL's product contains 85% of sumatriptan in the first layer. Specifically, the first layer of Par's ANDA tablet contains 100% of the tablet's sumatriptan, along with 15% of the tablet's naproxen, with the remaining 85% of the naproxen in the second layer.[15] DRL's ANDA tablet has 100% of the tablet's naproxen and 15% of the tablet's sumatriptan in the first layer, with the remaining 85% of the sumatriptan in the second layer.[16]

Par and DRL's arguments improperly focus on a literal comparison of the accused ANDA products to the Court's claim construction rather than an equivalents analysis to the claim. While

[15] *See* 10/14/10 A.M. TT at 13:21-25; PTX 91 at 230 (Par's product summary).

[16] 10/14/10 A.M. TT at 24:16-25:3; JTX137 at 18352 (DRL's product summary).

the Court's construction provides specific percentages, a strict, literal comparison of the accused product to the Court's construction undermines the purpose of the doctrine of equivalents. The proper inquiry is whether the accused value is insubstantially different from the claimed value. *See Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1292 (Fed. Cir. 2010). The recitation of a numerical value or range in a claim, absent more limiting language in the intrinsic record, does not preclude application of the doctrine of equivalents. *Id.* at 1292; *see also U.S. Philips Corp. v. Iwasaki Elec.Co.*, 505 F.3d 1371, 1378 (Fed. Cir. 2007) (concluding that "the doctrine of equivalents is not foreclosed with respect to the claimed concentration range"); *Abbott Labs. v. Dey, L.P.*, 287 F.3d 1097, 1100, 1105-08 (Fed. Cir. 2002) ("[t]he fact that a claim recites numeric ranges does not, by itself, preclude Abbott from relying on the doctrine of equivalents"); *Jeneric/Pentron, Inc. v. Dillon Co.*, 205 F.3d 1377, 1383 (Fed. Cir. 2000) (rejecting the argument that applying the doctrine of equivalents vitiates numerical claim limitations and concluding the doctrine of equivalents is available to a claim that recites a specific numeric range). While the Court's construction—not the claim—provides a range, this recitation of a numerical limitation does not preclude Pozen from relying on the doctrine of equivalents.

Likewise, the claim term "substantially all" does not foreclose Pozen from applying the doctrine of equivalents. *See Adams Respiratory*, 616 F.3d at 1292-93 ("at least 3500 hr*ng/mL" did not preclude application of the doctrine of equivalents). The words "substantially all" are an approximation, which serves only to expand the scope of literal infringement. *Id.; see also Philips Corp.,* 505 F.3d at 1379. Accordingly, the doctrine of equivalents is properly applied here, and its application does not vitiate the claim or the Court's construction.

In assessing equivalents, the Court considers whether Par's and DRL's ANDA products have the "same purpose, quality, and function" as claimed by the '183 patent. *See Atlas Powder Co. v.*

E.I. du Pont De Nemours & Co., 750 F.2d 1569 (Fed. Cir. 1984); *see also Graver Tank*, 339 U.S. at 611 ("Consideration must be given to the purpose for which an ingredient is used in a patent, the qualities it has when combined with the other ingredients, and the function which it is intended to perform."). The '183 patent is directed to a multilayer tablet whereby substantially all of the naproxen and triptan are segregated and separated for the purpose of independent dissolution. In applying the function, way, result test, the parties' experts generally agree that the function is to achieve separate, distinct layers of sumatriptan and naproxen. The way in which this function is achieved is by formulating the sumatriptan and naproxen in different manners to create physical barriers. The result is that substantially naproxen is separated from the naproxen, thereby providing independent dissolution.

Par's ANDA product performs essentially the same function: to achieve separate, distinct layers of triptan and naproxen by segregating the triptan and naproxen. 10/14/10 A.M. TT at 23:15-18; 10/14/10 P.M. TT at 90:22- 91:11. The segregation is achieved by formulating the sumatriptan and the naproxen in different manners, such as by using different compositions to create physical barriers. 10/14/10 A.M. TT at 23:19-22, PTX 90 at 224; PTX 183 at 109491, 109497-98. Specifically, Par achieves segregation by granulating 15% of the naproxen particles that are added to the first triptan layer. 10/14/10 A.M. TT at 19:14-24:22; PTX 90 at 224; PTX 91 at 230; PTX 183 at 109491; 109497-98. Par uses a polymer binder, PVP K-90, to form naproxen granules. *Id.* The PVP K-90 acts to ensure the coated naproxen has less interaction with the sumatriptan. *Id*. Par ANDA product has a first layer containing substantially all of the triptan and has the equivalent of a second, separate layer containing substantially all of the naproxen, and these two layers are in a

side-by-side arrangement.[17] *Id.* The result is that substantially all of the naproxen is separated and segregated from the sumatriptan, thereby providing independent dissolution. 10/14/10 A.M. TT at 14:13-15:5;18:2-19:13; 24:4-25:2; PTX 91 at 230, 469. Thus, Par's ANDA product performs the same function, the same way, to achieve the same result and satisfies the limitation under the doctrine of equivalents.

DRL's ANDA product achieves independent dissolution by the way it formulates and manufactures the tablets. DRL's ANDA product performs essentially the same function: to achieve separate, distinct layers of triptan and naproxen by segregating the triptan and naproxen. The naproxen particles in the second layer of DRL's ANDA product are granulated together with a PVP K-90 polymer binder. 10/14/10 A.M. TT at 29:23-30:5; JTX 115 at 18661. Then 15% of the sumatriptan is mixed with an aqueous PVP K-90 binder solution and sprayed onto the outer surfaces of some of these coated naproxen granules in the second layer. 10/14/10 A.M. TT at 28:16-29:8; JTX 115 at 18661. Thus, substantially all the triptan is segregated and separated into the equivalent of a first distinct layer, in an equivalent side-by-side arrangement, and this achieves the result of independent dissolution. 10/14/10 A.M. TT at 28:21-23, 27:4-28:7, 31:10-17; PTX 194 at 18562; JTX 115 at 18659-61. Moreover, DRL's testing of its ANDA product confirms its independent dissolution. 10/14/10 A.M. TT at 27:8-23; PTX194 at 18562. Likewise, DRL's ANDA product performs the same function, the same way, to achieve the same result and satisfies the limitation under the doctrine of equivalents.

This evidence of Par's and DRL's construction of and formulation of their ANDA products

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[17] Par and DRL also contend their ANDA products do not have defined, geometric layers as defined by the Court. The Court construed the term "a multilayer pharmaceutical tablet" as "a pharmaceutical tablet with at least two separate, distinct layers." Docket No. 257 at 22. This argument fails as there is an insubstantial difference between the construction of and formulation of Par's and DRL's ANDA products and the claim's requirment of "layers" and a "side by side arrqagement."

also establishes the insubstantial difference between their products and the claim's requirement of "layers" and "side by side arrangement." Par and DRL contend their ANDA products do not have defined, geometric layers as defined by the Court.[18] However, Par's and DRL's ANDA product summaries clearly describe the tablets' layer formation in addition to describing the various tablet layers. *See* 10/14/10 A.M. TT at 13:6-16, 13:21-25; PTX 91 at 230 (Par's Product Summary); PTX 97 at 481(Par's Pharmaceutical Development Report acknowledging a single layer dosage form was not feasible thus a bilayer tablet of sumatriptan and naproxen sodium was formulated); 10/14/10 A.M. TT at 26:17-27:23; JTX137 at 18352 (DRL's Overall Summary providing the describing its tablet's multiple layers comprising naproxen and triptan). Thus, this further shows that Par's and DRL's ANDA products also meet the disputed limitations under the doctrine of equivalents.

Finally, both Par and DRL argue their ANDA products are "admixtures," which Pozen specifically disclaimed during the '183 patent's prosecution. Par and DRL define an admixture as a tablet that has blended or mixed components. *See* 10/14/2010 at 37:17-19; Docket No. 400 at 54. Since they blend sumatriptan and naproxen, among other components, in forming their tablet layers, Par and DRL reason their products are admixtures and therefore cannot infringe under Pozen's prosecution disclaimer. *Id.*

Defendants' arguments, however, are inconsistent with Pozen's representation to the Patent Office. During prosecution, Pozen informed the Patent Office that "[t]he present claims require that naproxen and triptan be in a tablet in which they are segregated from one another in a 'side by side arrangement' and *in which their dissolution occurs independently of one another.*" JTX 5 at 1343884 (emphasis added). Pozen specifically disclaimed admixtures because they do not meet this

[18] The Court construed the term "a multilayer pharmaceutical tablet" as "a pharmaceutical tablet with at least two separate, distinct layers." Docket No. 257 at 22.

independent dissolution criteria.[19] Thus, Pozen defined admixtures as substances that do not achieve independent dissolution, not as substances with blended or mixed ingredients. *Id.* at 1343884-85.

However, as previously discussed, Pozen has shown by a preponderance of the evidence the accused ANDA products achieve independent dissolution. *See* Par: 10/14/10 A.M. TT at 14:13-15:5;18:2-19:13; 24:4-25:2; PTX 91 at 230, 469; PTX 183 at 109491, 109497-98; DRL: 10/14/10 A.M. TT at 27:4-28:7, 31:10-17; PTX 194 at 18562; *see also supra* at 24025.. Therefore, Par's and DRL's ANDA products cannot be admixtures since the intrinsic record defines "admixtures" by their lack of independent dissolution. Accordingly, Par and DRL do not escape infringement by categorizing their ANDA products as "admixtures" using a definition that falls outside the intrinsic record.

Neither Par nor DRL raise substantive non-infringement arguments regarding the remaining claim limitations. *See* 10/14/10 P.M. TT at 89:19-90:1; 10/15/10 TT at 11:19-12:4, 26:4-9. Thus, Pozen established by a preponderance of the evidence that these elements are satisfied. Specifically, Par's ANDA product literally meets the following elements of claim 2 of the '183 patent. Par's ANDA product is a multilayer pharmaceutical tablet, which is comprised of naproxen and triptan.[20] The said naproxen is in the form of naproxen sodium between 200 and 600 mg.[21] Par's ADNA product contains substantially all the triptan is in the first layer, since the first layer contains 100% of the sumatriptan, with 15% of the naproxen also in the first layer and the remaining 85% in the

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[19] Accordingly, in its claim construction opinion and order, the Court excluded admixtures from the claimed tablet architecture. Docket No. 257 at 21; *see also* JTX 5 at 1343884-85.

[20] *See* 10/14/10 A.M. TT at 13:6-16, PTX 97 at 481(Par's Pharmaceutical Development Report acknowledging a single layer dosage form was not feasible thus a bilayer tablet of sumatriptan and naproxen sodium was formulated).

[21] *Id*.; *see also* PTX109 at 9899 (Par's proposed package insert, providing the tablets contain 500 milligrams of naproxen sodium).

second layer.[22] Likewise, DRL's ANDA product is a multilayer pharmaceutical tablet comprising naproxen and triptan.[23] The said naproxen is in the form of naproxen sodium between 200 and 600 mg.[24] DRL's product summary describes the tablet as "bilayer" providing that it 100% of its naproxen, along with 15% of its sumatriptan, is in the first layer, and the remaining 85% of the sumatriptan is in the second layer.[25] Thus, substantially all of the naproxen is in a second, separate layer.

Based on the evidence set forth above, Pozen has shown by a preponderance of the evidence that Par and DRL infringe claim 2 of the '183 patent.

III. INVALIDITY

Defendants assert the asserted claims are invalid on multiple grounds. Defendants argue the '499 patent is invalid due to double patenting. Defendants also argue the '499, '458, and '183 patent are invalid as anticipated and obvious. Defendants further contend the '499 patent is invalid from the lack of written description.

A. Double Patenting

Defendants contend claims 5 and 15 of the '499 patent are invalid for double patenting if the claimed "therapeutic package" is just an "ordinary pill bottle." Docket No. 400 at 47. Defendants argue that claim 4 of the '499 patent, which claims the pharmaceutical composition, is not patentably distinct from claim 5 of the '499 patent, which claims a "therapeutic package" for the pharmaceutical

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[22] *See* 10/14/10 A.M. TT at 13:21-25; PTX 91 at 230 (Par's product summary).

[23] *See* 10/14/10 A.M. TT at 26:17-27:23; JTX137 at 18352 (DRL's Overall Summary providing the describing its tablet's multiple layers comprising naproxen and triptan).

[24] *Id.* (providing that Layer A contains 500 mg of naproxen sodium).

[25] 10/14/10 A.M. TT at 24:16-25:3; JTX137 at 18352 (DRL's product summary).

composition. Based on the premise that it is obvious that all pharmaceutical products are dispensed in a pill bottle, Defendants argue that claim 5 can only be a valid, non-obvious claim if the "therapeutic package" is something other than a standard pill bottle.

The double-patenting doctrine ensures the proper allocation of a patent term for an invention and prevents a patentee from obtaining more than one patent for the same invention or an obvious modification for the same invention. *In re Longi*, 759 F.2d 887, 892 (Fed. Cir. 1985). Obvious-type double patenting is a judicially created doctrine intended to prevent claims in separate applications or patents from claiming inventions so alike that granting both exclusive rights would effectively extend the life of patent protection. *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1373 (Fed. Cir. 2005).

Defendants argue obvious-type double patenting within the same patent: Defendants assert that claim 4 of the '499 patent is patentably indistinguishable from claim 5 of the '499 patent, thus claim 5 is invalid. This, however, is a misapplication of the doctrine. Double patenting applies to claims from separate patents, not the same patent, as the "fundamental" reason for the doctrine is to prevent an unjustified extension of the patent exclusivity rights. *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001). Accordingly, Defendants' argument fails. Claim 5 of the '499 patent is not invalid under the double-patenting doctrine.

B. Anticipation and Obviousness

Defendants collectively claim that the patents-in-suit are invalid due to anticipation and/or obviousness. Defendants claim that references Parma, Catarci, Saadah, the public treatment of four patients at Henry Ford Hospital, and the international Patent Corporation Treaty ("PCT") application WO 1998/06392, alone or in combination with additional prior art, invalidate the '458 patent and

'499 patents. Defendants also assert the that the '499 patent, combined with the Bandelin reference renders the '183 patent obvious.

1. Legal Standard

Defendants must present clear and convincing evidence to overcome the patents' presumption of validity. *Microsoft Corp. v. i4i Ltd.*, 131 S. Ct. 2238 (2011); *see* 35 U.S.C. § 282. A patent is invalid as anticipated if "the invention was patented or described in a printed publication in this or a foreign country . . . more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b). Although § 102 refers to "the invention" generally, the anticipation inquiry proceeds on a claim-by-claim basis. *See Hakim v. Cannon Avent Grp., PLC*, 479 F.3d 1313, 1319 (Fed. Cir. 2007). The single prior art reference must expressly or inherently disclose each claim limitation to anticipate a claim. *Finisar Corp. v. DirecTV Grp., Inc.*, 523 F.3d 1323, 1334 (2008). Additionally, the reference must "enable one of ordinary skill in the art to make the invention without undue experimentation." *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. 2009).

A patent claim is invalid as obvious "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). Although the ultimate determination of obviousness is a question of law, it is based on several underlying factual findings, including: 1) the scope and content of the prior art; 2) the level of ordinary skill in the pertinent art; 3) the differences between the claimed invention and the prior art; and 4) evidence of secondary factors, such as commercial success, long-felt need, and the failure of others. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

2. The ’458 and ’499 Patents

a. The Parties’ Invalidity Arguments regarding the ’458 and ’499 Patents

Defendants claim that the ’458 and ’499 patents are obvious to a person of ordinary skill in the art in light of Catarci (DTX 412), Parma (JTX 70), Saadah (DTX 400), the Henry Ford Patient Records 2, 5, 13, and 15 (DTX 378-79, 382-83), or the PCT application WO 1998/06392 (DTX 612), alone or in combination with additional prior art references. These references, except Catarci and the Henry Ford Patient Records, were before the PTO during the prosecution of the ’458 patent. JTX 2 at POZ01343987-POZ01343988. Defendants argue that the Parma and Catarci references each teach the concomitant administration of sumatriptan and naproxen and the Saadah and Raskin references together teach the combination of ergotamine and naproxen for the treatment of migraine, with the motivation to substitute sumatriptan for ergotamine. Defendants also contend the Henry Ford Patient Records show that doctors prescribed the combination of sumatriptan and naproxen for migraine patients. Defendants also generally contend that the ’499 limitations, requiring a “therapeutic package,” “finished pharmaceutical container,” and “labeling directing the use of said package” are obvious.

b. Invalidity Analysis of the ’458 and ’499 Patents

i) The Catarci Reference

The Catarci reference is a case report entitled “Ergotamine-induced headache can be sustained by sumatriptan daily intake.” DTX 412 at ParPharma 009885. Catarci describes a single migraine sufferer who developed ergotamine-induced headaches and subsequently replaced ergotamine with daily administration of sumatriptan. *Id.* Sumatriptan was “effective in alleviating episodic severe headache [sic] but did not relieve her constant, mild head pain,” and the patient continued to have daily migraines that were only relieved by sumatriptan. *Id.* Catarci discloses that

the patient was subsequently withdrawn from sumatriptan and "[n]on-steroidal anti-inflammatory drugs (NSAIDs) were [then] prescribed both on a daily basis and when required." *Id.* "Four weeks later [the patient] reported three migraine attacks per week, treated either with NSAIDs im [intramuscular] or sumatriptan sc [subcutaneous]." Catarci discloses that "[n]one of these [treatments] produced benefit." *Id.* Catarci further describes that the patient resumed taking daily doses of sumatriptan in addition to receiving acupuncture and the patient's migraine attacks were "promptly aborted by one tablet of sumatriptan." *Id.* Finally, Catachi concludes that "this case illustrates that acupuncture is occasionally of benefit in treating drug-induced daily headache." *Id.* at ParPharma 009886.

Defendants contend the Catarci reference renders obvious the asserted claims of the '499 and '458 patents. However, contrary to Defendants' contentions, Catarci does not teach the combination of sumatriptan and naproxen provided migraine relief to the patient. Rather, the reference teaches combining sumatriptan and acupuncture to treat migraine patients. *See Ricoh Co. v. Quanta Computer Inc.*, 550 F.3d 1325, 1332 (Fed. Cir. 2008) (a reference teaches away when "a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant"); *see also Iron Grip Barbell Co. v. USA Sports, Inc.,* 392 F.3d 1317, 1322 (Fed. Cir. 2004). Moreover, Catarci does not disclose longer lasting efficacy or reduced migraine relapse from the combination of sumatriptan and naproxen. Thus, the '458 and '499 patents would not have been obvious to one of ordinary skill in the art in light of Catarci.

ii) The Parma Reference

Parma is an Italian language reference entitled "The treatment of migraine: a study in general medicine." JTX 70. The Parma reference, with an English translation, was before the Patent and

Trademark Office ("PTO") during the '458 patent's prosecution. 10/12/10 p.m. TT at 153:12-153:14; JTX 2, 70. Parma is an epidemiological survey of migraine sufferers that assesses various migraine treatments. JTX 70. Parma listed the data collected and analyzed by the study in various tables. *Id.* A table labeled "Table VI. Combinations: 2 drugs" lists "FANS + sumatriptan"[26] and provides that "[t]he cornerstone of treatment is now still represented by FANS, both in monotherapy and in combination therapy." Parma also discloses "Table VIII. 'Unsatisfactory' treatments," which lists treatments using monotherapies, including the monotherapy of sumatriptan, and provides the percentage of "unsatisfactory" treatments received by the patients using monotherapies.

At trial, Pozen presented a declaration from one of the authors of the Parma reference, Dr. Tognoni. PTX 254. Dr. Tognoni is a medical doctor and clinical researcher at the Mario Negri Institute in Milan, Italy. *Id*. at 1. Mr. Tognoni was not retained as a consultant by Pozen, nor did he receive compensation for his declaration. *Id*. Dr. Tognoni stated that his publication does not suggest taking sumatriptan at the same time as another medicine, such as an LA-NSAID. *Id.* at 1-2. Dr. Tognoni further states that "[w]hile my article speaks of the 'associazone' [translated one way as combination therapy] of many pairs of drugs, including NSAIDs and sumatriptan, this is not meant as a reference to administering those two drugs at the same time, such as in a unit dose form, or together. Instead, when my article refers to the 'associazone' of drugs, it refers to the common practice of that time of migraine patients taking drugs separately in sequence, with a required gap in time between the administration of the drugs to determine the efficacy of the first drug before trying additional drugs." *Id.* at 3. Likewise, Pozen's expert, Dr. Blumenfeld, testified consistently with Dr. Tognoni's declaration. Dr. Blumenfeld testified that at the time of the invention, a person

[26] FANS is the Italian abbreviation for NSAIDs. 10/12/10 p.m. TT at 154:7-154:9.

of ordinary skill in the art would have interpreted these statements in Parma as disclosing the sequential administration of the various drug combinations. 10/12/10 p.m. TT at 154:2-154:17. Accordingly, Dr. Blumenfeld noted that "Table VI. Combinations: 2 drugs" refers to many drugs that would not have been administered simultaneously, such as two NSAIDs. *Id*. at 154:20-155:11.

On the other hand, Defendants' expert, Dr. Ramadan, offered a contrary opinion. Dr. Ramadan asserted that the reference teaches simultaneous administration and dismissed Dr. Blumenfeld's reasoning that Parma's inclusion of two NSAIDs in the Table VI shows that the administration was not concomitant. 10/14/10 a.m. TT at 104:15-105:4. JTX 70. To justify his position, Dr. Ramadan testified that "FANS and FANS [or NSAIDS and NSAIDs] are used in acute treatment of migraine as evidenced by clinical practice and the literature." 10/14/10 a.m. TT at 104:15-105:4. In addition, Dr. Ramadan testified that "Table VIII. 'Unsatisfactory' treatments" of the Parma reference indicated that the dissatisfaction would motivate a person of ordinary skill in the art to "[e]ither [administer] another agent or to [administer] combination therapy." 10/14/10 a.m. TT at 105:5-105:24.

Considering the parties' arguments and the evidence of record, Parma, in combination with what was known to a person of ordinary skill in the art before 1996, does not render the '458 or the '499 patent obvious. While Parma lists "FANS + sumatriptan" in "Table VI. Combinations: 2 drugs," taking the entire article in context, and as viewed by a person of ordinary skill in the art at the time of the invention, the reference does not teach simultaneous administration of naproxen and sumatriptan. Nor does Parma teach the combination of sumatriptan and naproxen produces longer lasting efficacy or reduces migraine relapse compared to the administration of sumatriptan or naproxen alone. Likewise, Dr. Ramadan's testimony fails to show these claim elements, which were not expressly disclosed, were otherwise present in the prior art or would have been obvious to one

of ordinary skill in the art. Nor is the Court persuaded by Defendants' arguments that a person of ordinary skill in the art would become motivated to use the combination of sumatriptan and naproxen due to the dissatisfaction rate of patients using sumatriptan monotherapy listed in Table VIII of the Parma reference. In light of Pozen's evidence and assertions regarding the Parma reference, supported with credible testimony from the reference's author and Pozen's expert, Pozen demonstrated that Defendants' invalidity claims lack substantial merit. Parma, in combination with what was known to a person of ordinary skill in the art before 1996, does not render the '458 or the '499 patent obvious.

iii) The Saadah Reference

The Saadah reference, entitled "Abortive Migraine Therapy With Oral Naproxen Sodium Plus Metoclopramide Plus Ergotamine Tartrate With Caffeine" discloses the simultaneous delivery of a formulation of ergotamine (a 5-HT agonist), naproxen, metoclopramide, and caffeine. DTX 400. The Saadah reference discloses the purposes for the inclusion of each of these components: ergotamine as a pain agent, metoclopramide and caffeine as anti-emetics to reduce nausea that is typically exacerbated by ergotamine, and naproxen as an additional analgesic. DTX 400; 10/15/10 TT at 91:25-93:16.

Defendants argue that because sumatriptan was known to be more effective and better tolerated than ergotamine, a person of ordinary skill in the art would have been motivated to substitute sumatriptan for ergotamine as disclosed in Saadah.[27] DTX 400, 364; 10/15/10 TT at 92:9-93:21; 10/14/10 TT at 116:3-11. As such, Defendants reason that the substitution of sumatriptan would also eliminate the need to co-administer anti-emetics, likewise eliminating the inclusion of

[27] Defendants cite Raskin, entitled "Acute and prophylactic treatment of migraine: Practical approaches and pharmacologic rationale," with Saadah to support their claim that it was known that sumatriptan was more effective and better tolerated than ergotamine. DTX364 at 1889 (left col.).

caffeine and metoclopramide included by Saadah. *Id.* Finally, Defendants argue the remaining claim elements not expressly disclosed by Saadah would have been obvious to one of ordinary skill in the art.

Pozen acknowledges a person of ordinary skill in the art may have been motivated to substitute sumatriptan for ergotamine; however, Pozen argues that the substitution would also eliminate the need for naproxen as well. In support, Pozen cites a contemporaneous letter, written to the editor of the journal that published Saadah, recommending the removal of naproxen and caffeine due to the side effects noted in the Saadah reference. 10/15/10 TT at 95:1-20; JTX 152.

The Court is not persuaded that a person of ordinary skill in the art would find it obvious, after reading Saadah, to substitute sumatriptan for ergotamine, metoclopramide, and caffeine. This would require the replacement of three out of the four components disclosed in Saadah's formulation, and Saadah disclosed each as having a specific purpose. Nor is the Court persuaded that a person of ordinary skill in the art would find the remaining claim elements, such as the simultaneous administration of naproxen and sumatriptan for the purpose of prolonged efficacy, obvious in light of Saadah. Even considering the Saadah and Raskin references together, the references do not teach the combination of ergotamine and naproxen for the treatment of migraines, with the motivation to substitute sumatriptan for ergotamine. Accordingly, the Saadah reference does not render the '458 or '499 patent obvious to a person of ordinary skill in the art.

iv) The Henry Ford Clinic Patient Records

Defendants also argue that four patient records from the Henry Ford Clinic in Detroit render the '458 patent invalid. 10/14/10 p.m. TT at 107:9-15; DTX383 (Patient 15); DTX378 (Patient 2); DTX379 (Patient 5); DTX382 (Patient 13). The records disclose that patients were treated for migraines with a combination of sumatriptan and naproxen. *Id.* However, the records do not

indicate simultaneous administration of naproxen and sumatriptan, and Dr. Ramadan, who treated patients at the Clinic, testified he did not recall ever prescribing or giving a patient sumatriptan and naproxen simultaneously. 10/14/10 p.m. TT at 59:2-5; 10/15/10 TT at 91:5-15. Nor is there any indication that one of ordinary skill in the art would view the patient records to teach or suggest the administration of sumatriptan and naproxen simultaneously. 10/15/10 TT at 91:14-91:24. Accordingly, the patient records do not render the '458 and '499 patents obvious to a person of ordinary skill in the art.

v) The WO Reference

Defendants argue that WO1998/06392, an international patent application published on February 19, 1998 under the PCT, anticipates the '458 patent. DTX 612. Defendants argue that the '458 patent is not entitled to claim priority to any of the prior applications because the '458 patent defines "concomitant" or "concomitantly" differently than the prior applications. Defendants' support for their position is the Court's different claim constructions regarding "concomitant" in the '458 patent and "concomitantly" in the '499 patent. Docket No. 257 at 10-14.[28]

The '458 patent claims a unit dosage form of sumatriptan and naproxen that is simultaneously administered to a patient for the treatment of migraines. The '458 patent claims priority to the originally filed claims and specification of application No. 60/024,129 (the "'129 application"). JTX 131. The '129 application discloses the simultaneous administration of a composition with therapeutically effective amounts of sumatriptan and naproxen to treat a migraine.

[28] The Court construed "concomitantly administering" and its permutations in the '499 patent as "simultaneous administration," or "administration of a second drug for migraine relief while a first drug for migraine relief is present in a therapeutically effective amount," or "administration of a 5-HT agonist and NSAID such that the effective plasma levels of the NSAID will be present in a subject from about one hour to about 12–24 hours after the onset of migraine or onset of precursor symptoms of a migraine." *Id.* at 10-13. The Court construed "concomitantly" and its permutations in the '458 patent as "given in close enough temporal proximity to allow their individual therapeutic effects to overlap." *Id.* at 13-14.

Moreover, Example 1 of the '129 application discloses each element of the asserted claims of the '458 patent. JTX 131 at POZ01276682. While the Court's constructions of "concomitant" and "concomitantly" are different, the '129 application discloses every element of the asserted claims of the '458 patent and thus supports Pozen's priority claims. Accordingly, the effective filing date of the '458 patent is August 16, 1996, thereby rendering WO1998/06392 inapplicable as prior art.

Defendants also dispute that the evidence of objective indicia supports non-obviousness, arguing that Treximet did not meet any unmet needs, it was not a commercial success, it was not "meaningfully" recognized by the industry, and its results were not "unexpected synergy" since there was no unexpected results regarding the pk profile (the absorption of the drug in the blood) of the drug combination. Defendants also assert Treximet is not covered by the '499 patent because it does not contain "labeling directing the use of said package."

Despite Defendants' arguments to the contrary, the evidence of record indicates the '458 and '499 patents are not obvious and further supports the patents' validity. Treximet is a commercial embodiment of the asserted claims of the '499 and '458 patents.[29] Treximet has generated a substantial economic benefit for Pozen, generating over $26.5 million in profits. *See* 10/15/10 TT at 48:11-50:8. Treximet sales in the first quarter of 2010 were approximately $30 million, which

[29] Treximet meets each limitation the asserted claims of the '499 and '458 patents. 10/12/10 P.M. TT at 136:8-136:10; 136:19-136:21. Treximet is a tablet suitable for oral administration containing 500 mg of the LA-NSAID naproxen sodium, a pharmaceutically acceptable salt of naproxen, and 85 mg of the 5-HT agonist sumatriptan. *Id*. at 115:4-115:10; 116:5-116:13; 116:25-117:6; 119:18-120:16; 120:24-121:3; 121:13-121:18; PTX 214 at 259514; PTX 206 at 1358304-05; PTX 207 at 1358333. The half-life of the naproxen in Treximet is 19 hours, which is at least four hours. PTX 214 at 259514; 10/12/10 P.M. TT at 119:22-119:24; 120:3-120:10. Treximet's duration of action for amounts of naproxen comparable to 500 mg is seven-to-nine hours which is at least six hours. PTX 206 at 1358305; PTX 207 at 1358333; 10/12/10 P.M. TT at 119:25-120:6. Because the sumatriptan and naproxen are in a single tablet, they are necessarily simultaneously administered to a patient, which produces longer lasting efficacy and reduces migraine relapse compared to the administration of either alone. 10/12/10 P.M. at 115:21-116:4, 121:13-121:18, 122:9-122:12; PTX 214 at 259514, 259519, 259536. Thus, Treximet is useful in treating a migraine patient. *Id*. Treximet also comes in a"finished pharmaceutical container," with labels that direct the patient to the medication guide or package insert prescribing information which in turn directs the patient to take a Treximet tablet to treat a migraine. 10/12/10 P.M. TT at 129:13-130:12; 133:24-135:7; PTX 214 at 259536-37, 259539; PTX 336.

was a market share in the triptan class of 7.1%. *Id.* at 45:1-45:24. Also during the first quarter of 2010, Treximet had 2.1 million patient days (the number of patients times the number of days on the therapy) and 149,000 prescriptions. *Id.* at 47:9-47:25. The patient days and total prescriptions represent shares of 5% or more in the triptan market. *Id*. at 45:19-46:4. Pozen presented evidence that this success is due to the patented features of the claimed invention, specifically the simultaneous administration of sumatriptan and naproxen, which produces longer lasting efficacy and reduced migraine relapse compared to either given alone. *Id*. at 54:14-55:11; *see also* PTX 409 at 12132 (FDA regulated marketing materials emphasizing the patented features). Accordingly, this demonstrates Treximet's commercial success.

In addition, at the time of the invention, the patented invention was contrary to the accepted practices for migraine therapy. At the time, practitioners were using first naproxen or other NSAIDs, and if they failed, practitioners sequentially used sumatriptan as a monotherapy to continually treat the relapse. *See* 10/13/10 A.M. TT at 23:15-24:1. Practitioners were not using naproxen and sumatriptan together at the start of an attack. *Id.* In an effort to solve recurrence, others in the art were exploring the use of re-dosing with sumatriptan, reformulating sumatriptan, or developing new triptans. *See* 10/12/10 P.M. at 81:14-82:21, 145:12-147:15; JTX 119 at 8956; JTX 149 at 12748, 12752; JTX 135 at 1365389; JTX 120 at 26109. Similarly, GSK initially rejected combining sumatriptan and naproxen and only decided to pursue Treximet after the Phase II clinical trial data was realized. *See* 10/12/10 A.M. TT at 97:11-97:21; Dr. Plachetka, 10/12/10 P.M. TT at 5:6-5:22; *see also* PTX 498. Pozen also argued that Treximet met a long-felt need as the first triptan approved by the FDA under the 24 hour sustained pain-free standard (as opposed to one or two hour pain relief). 10/13/10 A.M. at 25:3-25:15. Accordingly, the secondary considerations of the '458 and '499 patents support the patents' non-obviousness and validity.

vi) Conclusion

Considering the record and the parties' arguments, the Court does not find the prior art references invalidate the '458 and '499 patents. The references, separate or in combination, do not teach or suggest the simultaneous administration of sumatriptan and naproxen. Nor do the references teach or otherwise disclose to one of ordinary skill in the art that the combination of sumatriptan and naproxen produces a longer lasting efficacy reducing migraine relapse compared to the administration of naproxen or sumatriptan alone. Defendants failed to rebut the '458 and '499 patents' presumption of validity by clear and convincing evidence.

3. The '183 Patent

a. The Parties' Invalidity Arguments regarding the '183 Patent

Defendants also assert the '183 patent is obvious in light of the '499 patent, combined with Bandelin (JTX110) and/or the knowledge of a person of ordinary skill in the art. Defendants assert that multilayer tablets were well known in the art. JTX 110 at 12649-50; 10/14/10 P.M. TT at 108:10-16. Defendants also argue that because naproxen has very low solubility in acidic environments, it would retard the dissolution of sumtriptan. 10/14/10 TT at 104:12-105:2; JTX109 at 27169. Based this incompatibility, and the teaching of Bandelin, Defendants argue that a person of ordinary skill in the art would have chosen a multilayer tablet when formulating naproxen with sumatriptan. 10/14/10 TT at 107:9-23; JTX110 at 12648.

b. Invalidity Analysis of the '183 Patent

During the '183 patent's prosecution, the Examiner initially rejected the application on grounds similar to Defendants' arguments. JTX 5 at 1343857-62. The Examiner relied upon an earlier Pozen patent, U.S. Patent No. 5,872,145 ("the '145 patent"), in combination with U.S. Patent No. 2,951,792 ("Swintosky") and U.S. Patent No. 701,438 ("Whyte"). *See* JTX 5 at 1343860-61;

JTX 80. The Examiner noted that "Swintosky is cited to exemplify that the concept of separating tablet ingredients into various layers to control drug delivery rates, prevent interference between the two compounds, etc., is notoriously old." JTX 5 at 1343860. The Examiner further cited to Whyte "to exemplify that tablets with different layers of separated incompatible agents have been known in the art since at least 1902, the issue date of the Whyte." *Id*. at 1343861. In response, Pozen recognized that the concept of layering drugs in a tablet was well established in the prior art. *Id.* at 1343884. Pozen distinguished its invention by asserting that:

> The present claims require that naproxen and triptan be in a tablet in which they are segregated from one another in a "side by side arrangement" and in which their dissolution occurs independently of one another. The claims are limited to one very specific tablet architecture. Among the dosage forms falling outside the claims are: admixtures; any dosage forms other than tablets; tablets in which one drug is in a core and surrounded by a layer or coating containing the second drug; and tablets containing multiple drug release pellets or microparticles. Applicants submit that there is nothing in the prior art that would lead one of skill to choose the claimed dosage form over many other possible choices.

Id. Pozen furthered this argument by referencing the examples provided in the application:

> Example 1 describes the making of a bilayer tablet that falls within the scope of the present claims as well as two dosage forms that do not: a tablet in which sumatriptan is in a film coat surrounding naproxen and a tablet in which naproxen and sumatriptan are in admixture. The dissolution characteristics of these tablets are then compared in Example 2.

Id. at 1343884-85. Pozen also argued the dissolution characteristics and dosage forms made the claimed invention distinguishable from the prior art. *Id*. at 1343885. Upon consideration of Pozen's arguments, the Examiner allowed the claims. *Id*. at 1343927 ("As stated [in Pozen's amendment and rebuttal], the claims are limited to one very specific tablet architecture. Applicant argues that an advantage of forming such a tablet is demonstrated in the Examples section of the application. The examiner has very carefully considered these comments."); *see also id.* at 1343919-29.

While Defendants' references differ, the content of Defendants' references and obviousness arguments mirror the comments in the Examiner's initial rejection. These obviousness concerns were circumvented by Pozen's arguments, and Pozen presently asserts similar arguments of non-obviousness. Considering the record and the parties' arguments, the Court does not find the prior art references invalidate the '183 patent. The references, separate or in combination, do not establish that it was obvious to a person of ordinary skill in the art to formulate the naproxen sodium and sumatriptan into a bilayer configuration. While multilayer tablets were commonly used, Pozen's dosage forms of naproxen sodium and sumatriptan were not obvious. 10/12/10 P.M. TT at 37:22-39:15. Nor do the references render obvious the specific tablet architecture as Pozen argued to the PTO and claimed in the '183 patent. Accordingly, Defendants failed to rebut the '183 patent's presumption of validity by clear and convincing evidence.

C. Written Description of the '499 Patent

Defendants contend the asserted claim of the '499 patent is invalid due to lack of written description, arguing the asserted claim terms are not supported by the originally filed claims.

Section 112, paragraph 1, requires that the specification contain a written description of the invention. 35 U.S.C. § 112, ¶ 1. "[T]he hallmark of written description is disclosure." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). The written description requirement serves to "prevent an applicant from later asserting that he invented that which he did not." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003). A specification adequately describes an invention when it "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharm.,* 598 F.3d at 1351. Compliance with the written description requirement is a question of fact. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). The patentee need not

follow any specific form of disclosure in providing a written description of the invention, and drawings alone may be adequate to satisfy the written description requirement. *Id.* at 1564.

Specifically, Defendants argue the specification and originally-filed claims of the '499 patent and the prior applications in the family do not specifically recite or otherwise disclose a "therapeutic package" and a "finished pharmaceutical container" as claimed in claim 5 of the '499 patent. Defendants argue that because "therapeutic package" and a "finished pharmaceutical container" are not conventional terms used by the industry, the common knowledge that pharmaceutical products are typically and routinely found in containers or packages is irrelevant and insufficient to support the written description.

As a preliminary matter, there is no requirement that the prior application describe the claimed subject matter in exactly the same terms as used in the claims. *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000). Also contrary to Defendants' arguments, the Court may consider the knowledge of persons skilled in the art in considering the sufficiency of the prior application's written description. *Vas-Cath*, 935 F.2d at 1563-64 ("the disclosure of the prior application must 'convey with reasonable clarity *to those skilled in the art* that, as of the filing date sought, [the inventor] was in possession of the invention'") (emphasis added).

The '499 and '458 patents are derived from the same parent application, sharing substantially the same specification. As previously discussed, the '499 patent teaches a method for treating migraines by concomitantly administering therapeutic amounts of sumatriptan and naproxen. '499 patent at 3:22-50. The patent discloses several dosage forms, including an oral unit dosage form. *Id*. at 4:1-4, 12:54-55, 15:12-17. Based on these disclosures, persons of skill in the art would know these pharmaceutical dosages are administered to a patient in containers or packages with labeling and inserts with dosage instructions. *Id.* Dispensing pharmaceutical products in containers or

packages is not a new or unpredictable concept. A person of ordinary skill in the art would know that medications are not simply handed out to patients. Rather, pharmaceutical products, like the claimed tablets, are routinely administered in containers or packages. *See* 10/15/2010 at 97:24-98:18. Moreover, the FDA requires container labeling, medication guides, and package inserts for prescription pharmaceutical products. *Id*. Thus, upon reading the '499 patent, one skilled in the art would understand the meaning of "therapeutic package" and "finished pharmaceutical container."[30] Accordingly, there is adequate written description to support the '499 patent's validity.

IV. UNENFORCEABILITY

Par and Alphapharm also claim that the patents are unenforceable due to inequitable conduct. Defendants argue that during patent prosecution, the inventors made material misrepresentations regarding clinical data with the intent deceive the PTO, thus rendering the patents unenforceable due to inequitable conduct.

A. Legal Standard

"Inequitable conduct resides in failure to disclose material information, or submission of false material information, with an intent to deceive, and those two elements, materiality and intent, must be proven by clear and convincing evidence." *Kingsdown Med. Consultants, Ltd. v. Hollister Inc.*, 863 F.2d 867, 872 (Fed. Cir. 1988); *see also Praxair, Inc. v. ATMI, Inc.*, 543 F.3d 1306, 1313 (Fed. Cir. 2008). Intent and materiality are separate requirements. *See Therasense, Inc. v. Becton, Dickinson & Co.*, ___ F.3d ___, 2011 WL 2028255 at *9 (Fed. Cir. May 25, 2011); *Hoffmann–La Roche, Inc. v. Promega Corp.*, 323 F.3d 1354, 1359 (Fed. Cir. 2003). But for materiality is required to establish inequitable conduct:

[30] While "therapeutic package" is not limitation, nevertheless, there is adequate written description supporting the term. *See supra* at Part II.B.2.a.

> This court holds that, as a general matter, the materiality required to establish inequitable conduct is but-for materiality. When an applicant fails to disclose prior art to the PTO, that prior art is but-for material if the PTO would not have allowed a claim had it been aware of the undisclosed prior art. Hence, in assessing the materiality of a withheld reference, the court must determine whether the PTO would have allowed the claim if it had been aware of the undisclosed reference. In making this patentability determination, the court should apply the preponderance of the evidence standard and give claims their broadest reasonable construction.

Therasense, 2011 WL 2028255 at *11. Because an actual "intent to deceive" is required, evidence that the applicant knew of a reference and decided not to submit it to the PTO does not prove specific intent to deceive. *See Star Scientific Inc. v. R.J. Reynolds Tobacco Co.*, 537 F.3d 1357, 1366 (Fed. Cir. 2008) ("the fact that information later found material was not disclosed cannot, by itself, satisfy the deceptive intent element of inequitable conduct"). Intent may be shown from indirect and circumstantial evidence. *Therasense*, 2011 WL 2028255 at *10. When examining intent, the alleged conduct must be "viewed in light of all the evidence, including evidence indicative of good faith." *Kingsdown*, 863 F.2d at 876.

B. The Parties' Inequitable Conduct Arguments

Defendants argue that Pozen presented misleading data to the PTO during the prosecution of the '458 and '499 patents. In response to a rejection from the PTO, Pozen submitted an Amendment and Response and a Declaration of Dr. Plachetka. Pozen also submitted two studies, a Pilot Study and a Naproxen Study, arguing the study data supported "a surprising, synergistic effect" of the combination of sumatriptan and naproxen. JTX6 at POZ01353110-16, POZ01353730-33.

Defendants also argue that Pozen presented misleading data to the PTO during the prosecution of the '183 patent. Defendants argue these "omissions and misrepresentations" were critical to the prosecution and allowance of the '183 patent. Docket No. 400 at 55.

C. Inequitable Conduct Analysis

The Pilot Study compared sumatriptan alone against the combination of sumatriptan and naproxen. JTX4 at POZ01341841. No patients in the Pilot Study took just naproxen; thus the Pilot Study permitted a comparison only of the combination against sumatriptan alone. JTX4 at POZ01341842. Pozen told the PTO it had data from a separate clinical study, the Naproxen Study, that included a naproxen-only treatment group. Pozen combined the data from the two studies to compare the 24-hour sustained response rates for all three treatments (i.e., sumatriptan alone, naproxen alone, and the combination of sumatriptan and naproxen). Defendants argue that Pozen made improper "adjustments" to the studies that resulted in an exaggeration of the "effectiveness" of the combination therapy Pozen sought to patent. Defendants contend that the percentage of patients who responded to the combination was 3% less than the sum of the percentage of patients who responded to each active agent alone, thus showing that the combination was not synergistic as Pozen stated. Defendants further argue these adjustments were highly material since Pozen argued the '458 patent was patentable over the prior art because of the advantageous combination of sumatriptan and naproxen and that applicants' deceptive intent can be inferred.

Pozen offered testimony that contradicts Defendants' claims. Pozen explained the testing data and that the representations made to the PTO of the analysis were accurate. 10/12/10 p.m. TT at 33:2-37:9; 94:13-103:1; 10/13/10 a.m. TT at 104:1-112:12;10/13/10 p.m. TT at 28:3-39:3. Dr. Plachetka, the named inventor on the '458 patent and Pozen's President, Chief Executive Officer, and Chief Scientific Officer, testified that multiple analyses of the Pilot Study data were presented to the PTO to provide as much information as possible about the studies. 10/12/10 p.m. TT at 34:15-36:5. Likewise, Mr. McNamara, Pozen's Vice President of Business Development, also testified that Pozen explained to the PTO the differences between the two studies, including how and

why the comparison was made. 10/13/10 a.m. TT at 105:20-107:7; 10/13/10 p.m. at 29:1-34:10. These witnesses' testimony was credible, and the evidence does not indicate that Pozen intentionally mislead the PTO. Accordingly, the Court does not find the '458 and '499 patents unenforceable due to inequitable conduct.

Defendants claim that during prosecution of the '183 patent, Pozen's arguments that its invention offered substantial advantages over other dosage forms constitutes inequitable conduct because information regarding dissolution and pk data was not disclosed. Defendants argue these "omissions and misrepresentations" were critical to the prosecution and allowance of the '183 patent. Docket No. 400 at 55. Defendants did not present any evidence that these representations were made with deceptive intent. Moreover, Pozen presented contrary evidence that the dissolution data was consistent with the representations made to the PTO. *See* 10/14/10 P.M. TT at 80:21-81:23; JTX45 at 478849; 51. Pozen's testimony was credible, and the evidence does not indicate that the applicants intentionally mislead the PTO. Accordingly, the Court does not find the '183 patent unenforceable due to inequitable conduct.

V. INJUNCTIVE RELIEF

Pozen requests the Court set the effective dates of the approval of Defendants' ANDAs after the patents-in-suit expire and permanently enjoin Defendants until the patents' expiration.

A. Legal Standard

A permanent injunction is appropriate where: 1) a plaintiff suffers an irreparable injury; 2) the remedies at law, such as monetary damages, are inadequate to compensate for that injury; 3) the balance of hardships between the plaintiff and the defendant warrants the entry of a permanent injunction; and 4) the public interest would not be disserved by a permanent injunction. *See eBay, Inc. v. MercExchange, LLC*, 547 U.S. 388, 391 (2006).

B. Injunctive Relief Analysis

1. Irreparable Harm and Other Remedies at Law

Pozen argues it will suffer irreparable harm if Defendants are not enjoined because Pozen will lose vital revenue and irreversible market share and will suffer price erosion. First, relying on a declaration from Dr. Plachetka, Pozen submits that the loss of revenue stream from the launch of Par's ANDA product alone would devastate Pozen. Under the Pozen-GSK agreement, once a generic copy of Treximet enters the market, the royalty rate on Treximet will decrease by 70% (from its current rate of 18% to 5%). Pozen argues that it relies on this revenue from Treximet to develop and commercialize products and the loss of this revenue could force Pozen out of business. Pozen further argues the revenue loss would disrupt its primary business objective of developing innovative therapies. Second, Pozen contends that the entry of Defendants' ANDA products would cause Pozen to lose sales and market share to the lower priced generic products. Pozen also agues entry of the ANDA products could force Pozen to lower the price of Treximet to maintain its market share.

As demonstrated by Pozen's agreement with GSK, the launch of a generic product would significantly affect Pozen's revenue stream. Such a reduction of revenue would subsequently impact Pozen's ability to allocate its resources to product development. Likewise, Pozen would be harmed from the introduction of Defendants' ANDA products, which at a lower cost, would undoubtedly affect Pozen's market share. Taken together, Pozen has demonstrated that without a permanent injunction, it would suffer irreparable harm. *See, e.g., Abbot Labs*., 544 F.3d at 1361-62 (affirming the district court's conclusion that price erosion from current generic competition did not negate irreparable harm from the market share and revenue loss upon the entry of another generic competitor); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1382-83 (Fed. Cir. 2006) (affirming the district court's finding of irreparable harm based, in part, on price erosion); *Purdue Pharma L.P.*

v. Boehringer Ingelheim GMBH, 237 F.3d 1359, 1368 (Fed. Cir. 2001) (likelihood of price erosion and loss of market position are evidence of irreparable harm).

The commercial entry of Defendants' ANDA products would launch a cascade of consequences that, as provided above, cannot be undone. Defendants' proposed ANDA products violate the of exclusionary rights of Pozen's patents-in-suit. Remedies at law, such as monetary damages, are inadequate to compensate for such consequences. Accordingly, monetary damages cannot adequately compensate for the commercialization of Defendants' infringing products.

2. Balance of Equities

The balance of equities tips in Pozen's favor. While Defendants argue that the delay of bringing their ANDA products to market delays their revenue generation, Defendants' ANDA products have not entered the market. As provided, Pozen will suffer irreparable harm upon the introduction of Defendants' proposed ANDA products.

3. The Public Interest in an Injunction

The public interest in a permanent injunction does not tip in favor of either party. The importance of the patent system is encouraging innovation, as the "encouragement of investment-based risk is the fundamental purpose of the patent grant, and is based directly on the right to exclude." *See Sanofi-Synthelabo*, 470 F.3d at 1383. Nor is the public harmed by a permanent injunction, as Treximet is readily supplied to patients. On the other hand, as Defendants contend, the public would benefit from their lower priced generic ANDA products. However, a reduction of cost to consumers is balanced by the possibility of premature elimination of Pozen's patent rights.

4. Conclusion

Based on the parties' written submissions and the evidence of record, and for the reasons stated above, the Court grants Pozen's request for a permanent injunction under 35 U.S.C. §

271(e)(4)(B). Defendants Par Pharmaceutical Inc., Alphapharm Pty Ltd., and Dr. Reddy's Laboratories, Inc. shall be enjoined from making, using, importing, selling or offering to sell their ANDA products in the United States or inducing others in the manufacture, use, import, offer to sell or sale of their ANDA products in the United States until the expiration of U.S. Patent Nos. 6,060,499 and 6,586,458. Defendants Par Pharmaceutical Inc. and Dr. Reddy's Laboratories are also enjoined until the expiration of the U.S. Patent Nos 7,332,183 patent.

VI. CONCLUSION

Based on the evidence set forth above, the Court finds as follows: 1) Par's, Alphapharm's, and DRL's ANDA products directly infringe claim 15, as dependant on claim 5, of the '499 patent; 2) Par's, Alphapharm's, and DRL's ANDA products also induce infringement of claim 15, as dependant on claim 5, of the' 499 patent; 3) Par's, Alphapharm's, and DRL's ANDA products directly infringe claims 11, 12, 24, 26, 27, 29, and 30 of the '458 patent; and 4) Par's and DRL's ANDA products infringe claim 2 of the '183 patent.

Defendants failed to rebut the '458, '499, '183 patents' presumption of validity by clear and convincing evidence; thus, the Court does not find the prior art references invalidate the '458, '499, '183 patents. Finally, the Court does not find the '458, '499, '183 patents unenforceable due to inequitable conduct.

The Court grants Pozen's requested relief, and Par, Alphapharm, and DRL shall be enjoined from making, using, importing, selling or offering to sell their ANDA products in the United States or inducing others in the manufacture, use, import, offer to sell or sale of their ANDA products in the United States until the expiration of U.S. Patent Nos. 6,060,499 and 6,586,458. Par and DRL are also enjoined until the expiration of the U.S. Patent No. 7,332,183 patent. The Court also sets the effective dates of the approval of Defendants' ANDAs after the patents-in-suit expire.

So ORDERED and SIGNED this 5th day of August, 2011.

LEONARD DAVIS
UNITED STATES DISTRICT JUDGE